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THE PATHOLOGICAL ANATOMY OF "PARATYPHOID FEVER."*

REPORT OF A FATAL CASE, WITH BACTERIOLOGICAL FINDINGS.¹

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WITH refinements in the technic of the clinical application of the agglutination reactions, together with the more frequent application of cultural investigation of the blood in typhoid and other febrile diseases, has come the observation of a distinct set of cases of typhoid-like character that are caused by organisms intermediate between the typhoid and the colon bacillus. As these cases are clinically less severe, as a rule, than are infections with the true typhoid bacillus, there have been but few fatal results. Hence there is little known so far about the anatomic features of this disease, and its anatomic relation to true typhoid. In view of the close correspondence of the intermediate organisms and the typhoid bacillus, and the similarity of the clinical course of the cases, it might seem probable that the anatomic changes would be similar, if not identical. Up to the present time there have been reported four fatal cases with autopsy, in which the clinical course was like that of typhoid, together with the one we are about to describe; and since these correspond fairly well with one another and present quite a distinct picture, it may be considered that enough material has been collected to permit of some conclusions as to the pathologic anatomy of paratyphoid infection. If these cases represent the usual results of such infection, which would most naturally be the case, then it seems that the anatomic lesions of paratyphoid are quite different from those of true typhoid. Autopsies have so far been reported by Strong (17), Longcope (10), and Sion and Negel (15) in 1902, and Lucksch (11) in 1903. Autopsies in which the paratyphoid organism has been

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recovered have also been reported by Schmidt (13) and by Libman (9), but these were cases in which the disease was quite unlike typhoid fever, that of Schmidt being in the nature of a pyemia following an infection of the bile tracts in cholelithiasis. Libman's (9) case is described by him as resembling a cholecystitis or liver abscess, so much so that operation was performed; at autopsy healed and healing ulcers were found in the ileum. As the patient's blood reacted with the typhoid bacillus, he considers the paratyphoid infection to have been secondary to a recovering typhoid infection of the ambulatory type, mixed infections having been mentioned by other writers.

It may be necessary at this point to discuss briefly the matter of terminology to be adopted in referring to these cases. In the cases reported there has been a more or less random use of the terms "paratyphoid" and "paracolon," the former term generally applying to the clinical disease, the latter more particularly to the biologic features of the causative organism. Buxton (4) has attempted a classification harmonizing these two aspects, based upon a comparative study of the bacilli, in the following words:

"The following classification is therefore suggested:

Paracolons.—Those which do not cause typhoidal symptoms in man. A group containing many different members, but culturally alike.

Paratyphoids.—Those which cause typhoidal symptoms.

a) A distinct species culturally unlike the paracolons.

β) A distinct species culturally resembling the paracolons."

In the reported cases of infection with the members of this group of organisms the clinical features have been very variable, from those indistinguishable in most respects from typhoid, to those in which the organism has been an accidental finding in abscesses, etc., without relation to such a disease, as in the case of Widal and Nobecourt. From the clinical side, therefore, it may be well to recognize as a separate group those cases that resemble typhoid, reserving for them the term "paratyphoid," and referring to the other cases properly as "paracolon infections," recognizing that, if Buxton's classification is correct, the same organism may be responsible in each. The situation then will not be at all

different from what it now is in relation to infections with the Eberth bacillus. In this article, therefore, the term "paratyphoid" will be used as above indicated, without reference to the particular variety of organism involved.

CASE I.

The first case is that of a soldier, who died in Santa Cruz, July 31, 1900, reported by Strong (17) two years later. His sickness began July 5, with fever and rectal discharges of blood and mucus. "No departure from the ordinary type of typhoid fever." On account of unfavorable conditions existing at the time of death, the case unfortunately could not be completely studied. Autopsy was held forty-two hours after death, and there was much post-mortem change. The mesenteric lymphatics were swollen, and some, along the small intestine, were hemorrhagic. The spleen was very large and soft, and the pulp somewhat dark and considerably increased in amount. The liver showed advanced fatty degeneration. The capsule of the kidneys was not adherent; the organs were pale and yellow in color. Both the large and small intestine were normal throughout, except for a moderate catarrh and a few superficial hemorrhages. The solitary and agminated follicles showed no lesions. The other organs were normal. Stained coverslips from the liver showed a large capsulated bacillus, considered to be *B. aerogenes capsulatus*, and a smaller bacillus. Fresh smears from the spleen showed a few concentric aestivo-autumnal parasites, and a fair amount of malarial pigment. From the spleen a pure culture was obtained of an organism with the following characteristics: Bouillon was at first clouded; after a time a sediment formed at the bottom and often a pellicle at the top; hanging drop showed a motile bacillus; stained coverslips decolorized by Gram's method; in glucose agar there was a moderate gas production; in lactose agar there was no gas production; saccharose was moderately fermented; litmus milk was at first reddened after fourteen to twenty-four hours, and then turned blue after about forty-eight hours; in Smith's sugar-free bouillon there was no indol production. This organism was pathogenic for mice. No serum of the patient was saved for testing, and no agglutination tests seem to have been made. The few malarial parasites are considered by Strong insufficient to account for the illness, particularly as the patient received quinine. There was no other evident cause for the death of the patient than infection with this bacillus. A further study of the organism isolated by Strong will be found recorded by Buxton, in his article already quoted.

CASE II.

(Reported by W. T. Longcope (10), from Philadelphia.)

An Italian laborer, twenty-two years old, suffered from a sickness of about eleven days resembling typhoid. There was epistaxis, herpes labialis and nasalis, palpable spleen, and rose spots. Fever was high, and there was delirium. The Widal reaction was negative. Leucocytes, 5,900. Blood cultures made the day before death yielded a typhoid-like bacillus. Autopsy

showed a flabby heart, otherwise unchanged. Lungs congested and edematous, but no areas of consolidation. Spleen weighed 460 g.; extremely soft; surface dull, reddish gray, with a few small hemorrhages. Liver weighed 1,810 g.; large, soft, showing cloudy swelling. Intestines showed no changes beyond slight enlargement of the solitary follicles in the colon, and the presence of *Ascaris lumbricoides* in large numbers. Mesenteric glands also free from changes, as were the other organs. Cultures from the heart's blood, lung, liver, and spleen gave an organism identical with the one isolated from the blood during life; no growths from the mesenteric glands, gall bladder, and cerebro-spinal fluid. The colon bacillus was also obtained from the liver.

Histologically the spleen was much congested, and the Malpighian bodies somewhat increased in size. There was no endothelioid proliferation, and no red blood-carrying cells were found. The liver showed, besides the general swelling and granulation of the cells, multiple focal necroses. In these foci cells of an epithelioid type were entirely absent, but leucocytes were present as well as fibrin. The capillaries contained few leucocytes and no thrombi. No definite lesions were found in the solitary follicles of the large intestines or in the Peyer's patches of the ileum; in one or two sections the lymphoid tissue was slightly increased, and in the germinal centers of the largest follicles one or two endothelioid cells were found. These cells occurred in no other situations in the intestinal wall. The mesenteric glands were unaltered.

CASE III.

(Reported by Sion and Negel (15), from Jassy, Roumania.)

This occurred in a man, twenty-four years old, who suffered from symptoms resembling typhoid, with cerebral manifestations, trismus, opisthotonus, paralysis of the right half of the body, and aphasia. The bacteriologic examination gave an organism corresponding with the paracolon bacillus. The anatomic findings were: Splenic swelling; parenchymatous degeneration; enteritis of a dysenteric character in the lower part of the ileum; a Laennec's vegetation in the left ventricle, with embolic foci of softening in the brain; infarcts in the spleen and kidney; bronchitis and pneumonia. As regards the intestine, it is stated that the entire intestinal mucosa was slightly reddened, while the lower part of the ileum and the ascending colon were darker red; the largest follicles were the size of millet seeds. At the lower end of the ileum the folds of mucous membrane showed gray, dirty bands, 1 mm. broad, for an extent of 10 cm., which were produced by a deposit of a bran-like material that was easily rubbed off, and under it the mucosa was less shining and deeper red. There was no swelling or ulceration of Peyer's patches whatever, nor of the solitary follicles, not even the slightest prominence or injection; the mesenteric glands were equally unaffected.

CASE IV.

At Prague during the winter of 1902-3 there was a large epidemic of typhoid, with the usual anatomic findings. There occurred one, however, in which the autopsy findings were so different from the usual picture that it seemed apparent to the examiner that he was dealing with something other than a true typhoid. Bacteriological examination showed that a paracolon

bacillus was the cause of the disease. The summary of the case, reported by Lucksch (11), is as follows:

The patient was a male, twenty-five years old, sick for a week before entrance to the hospital on December 24. The symptoms were chiefly weakness and depression; the stools became diarrhoeic, and four days before entering the hospital he had been in bed; for two days he had been unconscious. Examination showed the countenance bluish, the right conjunctiva reddened, the lips and tongue dry; the mouth would remain open. Abdomen much inflated. Spleen not palpable, but much enlarged on percussion. A few scattered rose spots on the abdomen. Bowels and bladder were emptied unconsciously; in the urine were albumen and indican. Death occurred in collapse on December 28, that is, about the twelfth day of the disease, the highest temperature recorded being on the 26th, when it reached 39° C. On the 26th the patient's blood gave, with strains of *B. typhosus*, a positive reaction in concentration of 1:40.

Autopsy was performed twenty-one hours after death. The abdomen was distended; visible mucous membranes pale; on the lower extremities punctate, large red flecks. Brain and meninges showed no changes. Diaphragm reached the fifth rib. Thyroid normal. Lungs adherent at the apices; studded over the lower lobe with small, pea-sized areas of consolidation, moist, dark red in color, and some a little raised. Pericardium normal. Heart unchanged, except pale and soft. The intestines were much distended. Liver small, soft, pale, and easily torn. No changes in the gall bladder. The spleen was slightly swollen, dark red, and soft. Kidneys pale and soft. Mucous membranes in general pale. The stomach showed a few hemorrhages in the mucosa. Small intestines much thinned (through distention), everywhere pale; neither solitary follicles nor Peyer's patches swollen. The mucosa of the large intestines was generally pale, in the cecum and ascending colon several spots where irregular transverse ulcers occurred, some with necrotic tissue shreds in the center. These occurred in groups of two or three, their margins not being swollen, and having an extent of up to 1 sq. cm. In the transverse colon the follicles, measuring 1-2 mm. in diameter, colored grayish yellow, were surrounded by a red margin 1 mm. wide. In the rectum and sigmoid flexure were no pathological alterations. The mesenteric lymph glands were generally of a dark red color, not enlarged, neither were the glands of the large intestines swollen, with the exception of one in the vicinity of the cecum, which was the size of a cherry. Pancreas and adrenals were normal.

Histology.—Liver: Slight fatty infiltration in the center of the lobules. The cellular cytoplasm was slightly granular. Spleen: Pulp elements slightly increased, but there was no demonstrable hypertrophy. Kidneys: No alteration except slight granular change in the cytoplasm. Lymph glands: In the swollen gland was an increase in lymph cells, and there were many enlarged endothelial cells with one, two, or more nuclei. No vascular congestion of the gland. Intestine: Follicles of the large intestine were not swollen, yet they contained much swollen endothelium. In the vicinity of the follicles was a slight round cell infiltration of the submucosa. The mucosa over the follicles was much infiltrated with round cells, but in places

there was still normal epithelium. Away from the follicles the submucosa showed no inflammatory reaction, and the muscularis was entirely free from it. Sections through the ulcers showed that here the mucosa and submucosa had entirely disappeared in some places, while in others there were still remains of Lieberkühn's crypts. All layers present, to the serosa, showed a moderate grade of round cell infiltration in the floor of the ulcers and for a short distance about them. There was no special swelling of the follicles in this vicinity. Blood-vessels were somewhat dilated. In places the ulceration reached to the muscularis. As the author remarks, these alterations lack the marked infiltration of the lymphatic apparatus of typhoid; they are more like those of dysentery, although not exactly the same. Bacteria were found in the ulcers, short bacilli in small numbers, that did not stain by Gram's method; but also in the superficial layers were cocci and large bacilli that retained the stain. Bacteria could not be found in the liver, spleen, kidneys, and lymph glands.

CASE V.

This case, which we desire to report, occurred in St. Luke's Hospital, Chicago, in the service of Dr. H. B. Favill, to whom we are indebted for the use of the clinical history. We also owe thanks to Dr. Gay for help in preparing the record. The patient, C. H., was a carpenter, aged forty, who entered the hospital June 9, 1903, complaining of hemorrhage from the bowels and general malaise. His sickness began two weeks before entrance with pains and stiffness in the back and legs, dull headache, and gradual loss of appetite. During this time constipation persisted for about the first six days; nine days before entrance there occurred several hard movements, not accompanied by griping. The next day he took to bed. Early on this day he vomited. He suffered no localized pain. His strength gradually decreased, and during the second week of the illness there was a hacking cough. On the morning of entrance he had a bowel movement containing much fresh blood; this was not painful or preceded by pain. He had been practically free from sickness previous to this illness, and his habits and general history were good.

Examination showed some emaciation; color pale, "muddy;" conjunctiva slightly yellowish; aspect listless, dull, but not distinctly typhoid. Circulatory system negative, except for a typical dicrotic pulse; as also was the respiratory system, except for a slight hacking cough. Tongue was dry, fissured, and covered with a blackish-brown coat; protruded slowly, with tremor. The

liver was not enlarged. Spleen barely palpable at the costal margin, and slightly tender. The entire abdomen was distended, giving a tympanic note on percussion. The skin was dry over the body, but covered with sweat over the neck and face. On the abdomen were one or two "rose spots," 2-3 mm. in diameter. Except for rachitic tibiae, the physical findings were otherwise practically negative. The urine contained from the first considerable albumin, hyalin, and granular casts, and much indican. Widal tests were made on June 9, 12, 14, and 20, all of them being negative with a dilution of 1 to 40. On June 9 the leucocyte count was 5,400; on June 12, 7,400; on June 24, 5,000. On the 24th the hemoglobin was at 70 per cent.

On the day of entrance the temperature remained at about 104° with pulse of 100 to 110, and respirations from 20 to 26. The first night, which was the fifteenth day of the disease, there was again a passage of a large amount of blood in the feces, and there were further discharges of blood during the first three days' stay in the hospital; but not later. Later the stools resembled those common in typhoid fever. The temperature was not so high during the rest of the illness, although it did occasionally reach 103°. There was occasional emesis, and on the thirtieth and thirty-third days chills occurred, followed by a rise in temperature. Death occurred on June 27, about the thirty-third day of the disease.

The subjective clinical features of this case were: (1) absence of depression; (2) absence of any active or low muttering delirium, except during the first three nights in the hospital, and the few days immediately previous to death; (3) the relatively high pulse in the last two weeks.

AUTOPSY

The autopsy was performed about seventeen hours after death. The body was that of a poorly developed, emaciated man, 151 cm. tall. Sclera white. Superficial lymph glands not enlarged. Both tibiae curved forward in the median part, with transverse flattening. Toe nails greatly deformed (onychogryphosis). There was a large bed sore over the sacrum, and a smaller one beginning over the left scapula. Subcutaneous fat was almost entirely absent.

Abdominal cavity.—Inguinal and femoral rings closed. Omentum almost devoid of fat. A few adhesions about the spleen. Appendix 5 cm. long, free from adhesions. Mesenteric lymph glands not enlarged or congested, and appear of normal consistence. The liver reaches just to the costal margin. The peritoneum is everywhere smooth and shining; there is no discoloration of the intestinal covering, except a slight reddening over the ileum just as it joins the colon. No abnormal fluid in the cavity. Retroperitoneal glands not enlarged. A few adhesions about the gall bladder, but none about the liver.

Thoracic cavity.—Both pleural cavities are free from adhesions, except a few to the pericardium, and there is no increased amount of fluid. At the site of the thymus there is a small amount of pinkish tissue. The pericardial cavity contains 30 c.c. of clear fluid; surface smooth and shining, except for a "milk spot" on the anterior surface of the right ventricle, about 5×2 cm.

Heart.—Valves, orifices, and endocardium normal in all respects. Musculature of normal consistence, but slightly pale; no increase in the connective tissue; both ventricles slightly dilated.

Lungs.—The lungs are soft and pale in the anterior portion; much darker and more firm posteriorly. Beneath the pleura are many small ecchymoses. Cut surface exudes much frothy fluid, that from the posterior part being mixed with blood. Near the posterior margin of the left lower lobe is an area 1 cm. in diameter projecting from the surface, which is quite firm, with a pale center and dark red periphery; upon cutting this open the center is white and extends 4 mm. into the lung substance, firm and flesh-like in consistence. Near the hilum of the right lung was a small puckered scar with a grain of calcareous material in the center.

Thyroid.—Not enlarged; contains little colloid.

Liver.—Of moderately firm consistence, and contains a large amount of blood. Cut surface shows lobular markings plainly; peripheries light in color.

Spleen.—Greatly enlarged, being over twice as large as normal; weight 400 g. Consistence extremely soft, and it tears very

easily. Cut surface is dark in color; Malpighian bodies difficult to discern; pulp is almost fluid in consistence.

Pancreas.—Shows no changes.

Gastro-intestinal tract.—Stomach and esophagus show no changes. In the ileum, just above the ileo-cecal valve, ulcerations are encountered. In the lowest 3 cm. of the ileum the mucosa is almost entirely ulcerated away, and the ulcerations extend upward with less abundance to a height of 8 cm. The ulcers are extremely irregular in size and shape, often coalescing, so that there are but a few separate ulcers to be distinguished. They bear no relation to the lymphatic apparatus of the bowel, but stop abruptly with the margin of the ileo-cecal valve. The floor of the ulcers does not show the muscularis in any place, although the mucosa has been ulcerated through and removed; the floor is of a dirty gray color, but there seems to be no deposition of any sort of membrane. The margins are not in the least swollen, although often slightly undermined. The bowel near the ulcers is not at all swollen or hyperemic, except a diffuse reddening just at the junction of ileum and colon. The peritoneum is not affected. The ulcerations are entirely dissimilar to those of typhoid, particularly in the lack of infiltration and in their superficiality; they resemble much more the ulcers of dysentery. Twenty-six cm. above the valve is a solitary area of swelling, with beginning ulceration, and 60 cm. above is still another. The solitary follicles, except for these areas, are not at all enlarged, and Peyer's patches are equally free from any swelling whatever—they can be found only with difficulty. As a whole, the walls of the intestine seem thin and pale. In the large intestine there is no ulceration, and no enlargement of the follicles. The mucosa of the appendix also appears normal.

Kidneys.—A little enlarged, weighing 180 g. each; consistence firm; no external changes. Cut surface dark in color, because of the presence of much blood; cortex measures 6-8 mm. in thickness, the markings being fairly distinct. The capsule strips, leaving a smooth surface. The adrenals, urinary bladder, and prostate show no changes.

HISTOLOGICAL EXAMINATION.

Intestine.—Sections taken through different ulcers show that in general the ulceration extends into the submucosa, but rarely passes through it. There seems to have occurred some post-mortem digestion of the surface. The margin of the ulcers is usually sharp, often slightly undermined, and passes abruptly through the mucosa, generally to about the middle of the submucosa. The chief feature is the absence of any evidence of reaction in the ulcerative process. The floor and margin of the ulcer is formed by tissue that has lost all affinity for nuclear stain, although retaining in part the form of the cells that originally composed it, and which stain faintly with eosin. This non-staining part fades insensibly into the tissue that appears quite normal. This absence of demarkation is similar to that seen in noma and other gangrenous ulcerative lesions. Where the margin of the ulcer passes through a lymph follicle the cells at the margin of the necrotic part are obscured by a diffuse dark blue stain, as if the nuclear substance of the lymphoid cells had diffused among them, still retaining its affinity for stain. Except for this, the presence of the lymphatic structures does not seem to have any effect on, or relation to, the ulcerative process. The portions of tissue adjacent to the ulcer seem almost entirely unaffected by the process. There may be a few more plasma cells than normal, but there is no congestion. The lymph follicles show a total absence of the endothelial proliferation of typhoid fever, phagocytes can rarely be found, and there are no thrombi except in the necrosed tissue. There are a few small hemorrhages in the submucosa, but they are rare. There is also a total absence of leucocytic invasion, and there are very few eosinophiles to be found in the tissues.

Stained by methylene blue, the tissues beneath the floor of the ulcer are found to be swarming with bacteria. On and near the surface are bacilli of various shapes and sizes, spored and non-spored, and a few cocci. Penetrating deeper into the tissue, but rarely beneath the submucosa, are bacilli of the shape and size of long colon bacilli. This bacterial growth is quite diffuse, without tendency to form colonies. Stained by Gram's method, only part

of the surface forms can be seen—few bacteria beneath the surface retain the stain—the long bacilli being quite decolorized.

Mesenteric glands.—There is a total absence of congestion or swelling of the lymph follicles and sinuses. In the sinuses, however, are numerous small areas filled with fibrin and containing few cells. They resemble focal necroses, except for the absence of any remnants of necrotic cells or cellular infiltration. The cells immediately about them are unaltered, and the fibrin passes off in threads between the cells of the normal tissue. Occasional small threads of fibrin can be found in many places in the glands. In the lymph sinuses there is some increase in the number of endothelial cells, but by no means comparable to that seen in typhoid. A few of them contain a single lymphoid cell, but phagocytosis is by no means common. There are many plasma cells in the sinuses, and a few polymorphonuclear leucocytes. The blood vessels contain many leucocytes and occasional plasma cells. The germinal centers of the follicles show no evidence of proliferation. Sections were stained by Gram's method and with methylene blue, but no bacteria could be found.

Liver.—In general the liver cells are unchanged, except that those near the center of the follicle contain a golden-brown pigment usually situated in the center of the cells. A few small but typical foci of necrosis are present, in which the destroyed liver cells have been replaced chiefly by small mononuclear cells, a few leucocytes and plasma cells, and what in some instances appear to be new-formed liver cells. Such areas are scanty, and all are small. They differ from the foci of typhoid chiefly in the absence of endothelial cells. Between the liver-cell columns are more than the usual number of polymorphonuclear leucocytes. There is no congestion or connective tissue proliferation, and bile-vessels and blood-vessels appear unchanged. In the capillaries are frequently found clumps of bacteria of the form of the colon type; they are destained by Gram's method. There is no change observable in the cells immediately in contact with these masses of bacilli, so it would seem probable that they have multiplied after death.

Spleen.—Here the changes are much like those of acute

splenic swelling of typhoid. There is the same separation of the Malpighian bodies by the congested splenic pulp, in some areas of which nothing at all can be seen but blood, as if a parenchymatous hemorrhage had occurred. In the pulp are many large endothelial cells, many of which are full of a golden-brown pigment, others containing red corpuscles in various stages of destruction, and lymphoid cells. There are many polymorphonuclear leucocytes, some of which contain pigment, and an increased number of plasmic cells. The increase in the number of cells in the pulp is so great that it seems that the increased size of the spleen is due as much to them as to the blood. No changes are seen in the Malpighian bodies, vessels and stroma. No areas of focal necrosis were found, and no bacteria could be found in sections.

Kidneys.—Except for congestion of the tufts there are no changes in the glomerules. The convoluted tubules have a low epithelium with nuclei generally small and deep-staining; the lumen is filled with granular, eosin-staining detritus. The collecting tubules are approximately normal and free from casts. The capillaries are generally distended, particularly in the medulla. No interstitial increase has occurred.

Adrenals.—No changes are found, in spite of the fact that many of the small vessels are filled with bacilli that are destained by Gram's method. The cells in the vicinity of the bacilli do not seem affected thereby. There seem to be a few more plasma and round cells in the interstitial tissue than is usual.

Lung.—The nodule found in the lung histologically presents the features of a small septic infarct. There is a central mass of leucocytes, among which are practically no remains of the lung tissue, and outside is a wide area in which the air sacs are packed with well-preserved red corpuscles. Beyond this the lung presents no features of special interest, the findings being those of hypostatic congestion and compensatory emphysema.

Myocardium.—Beyond a slight segmentation of the muscle fibers there are no changes.

Pancreas.—Except for small fibrinous thrombi in the large veins there are no changes.

Thyroid.—Presents no alterations.

Thymus.—There is quite a large amount of thymus tissue present in the lobules of fat that usually replace it, but only traces of Hassell's corpuscles remain.

Prostate.—The tubules are packed with desquamated cells, and there is a slight increase in the round cells of the muscular portion.

ANATOMIC DIAGNOSIS.

Multiple ulcerations in the mucosa of the ileum; pulmonary edema, hypostatic congestion, and compensatory emphysema; acute splenic swelling; septic infarct in the lung; chronic nephritis with congestion; decubitus; rachitic tibiae; onychogryphosis; paracolon bacillemia; focal necroses in the liver.

BACTERIOLOGICAL REPORT.

At autopsy cultures were made from the heart's blood, liver, spleen, and kidney. The heart's blood gave a mixed culture of a small bacillus and a staphylococcus. The cultures from the liver remained sterile, while those made from the spleen and kidney gave a pure culture of a short, actively motile bacillus. The latter organism has been found to belong to the group intermediate between the colon and the typhoid groups, *i. e.*, to the group of which *B. enteritidis* of Grtner, *B. psittacosis*, the paracolon bacillus described by Gwyn, and Cushing's bacillus O: are members.

The cases of paratyphoid infection, reported by Achard and Bensaude (1), Widal (18), Gwyn (7), Cushing (6), Schottmller (14), Brion and Kayser (3), and others, have been so fully reviewed by Buxton, and more recently by Korte (19), that it seems unnecessary to go into detail.

G. Bernard Smith (16) has recently reported two cases of paratyphoid fever from both of which organisms belonging to the intermediate group were isolated. The organism from Case I produced gas in glucose, but not in lactose, saccharose, maltose, mannite, levulose, or dextrin. From Case II the organism produced gas in glucose, maltose, mannite, levulose, and dextrin. The organism from Case I, although undoubtedly a member of the

intermediate group, differs from the organisms isolated from all other reported cases in that it produces free gas in dextrose only. In maltose, mannite, and levulose growth occurred in the closed arm of the fermentation tube, but no free gas was produced.

Buxton (4) divides the members of the intermediate group into the paracolons, or those which do not produce typhoidal symptoms in man, and the paratyphoids—those which do produce such symptoms. This latter group is subdivided into:

Group α . A distinct species, differing from the paracolons in cultural characteristics. These organisms produce acid in milk, and the medium becomes alkaline in about ten days; gas is produced in yeast and glucose broths, with no increase in the amount after the first twenty-four hours; the color in neutral red agar changes completely to yellow in forty-eight hours, this color being permanent. Sera of animals immunized against members of this group give interactive agglutinations within the group, but give negative results when tested with members of Group β .

Group β . The organisms belonging to this group culturally resemble the paracolons. Permanent acidity is produced in litmus milk; gas is produced in yeast broth, the amount increasing up to the third day; a yellow color appears in neutral red agar after forty-eight hours, the original red color returning after four to five days. Agglutination tests were interactive within the group only.

BIOLOGICAL AND CULTURAL CHARACTERS OF BACILLUS FROM THE PRESENT CASE.

The organism obtained from the spleen and kidney was a short, actively motile bacillus, which was decolorized by Gram's method. The growth of the organism on agar, gelatin, broth, and potato does not differ from the growth of the typhoid bacillus.

On agar a white growth appears along the path of the needle. Gelatin is not liquefied. Peptone broth becomes clouded, but there is no pellicle formed and no sediment. Indol is not formed. Potato shows a slight growth, with no discoloration.

Milk is rendered slightly acid in from two to five days, and then changes slowly to an alkaline reaction which is pronounced

after from ten to fourteen days. A slight opalescence appears about the seventh day.

Gas production.—In testing for gas formation, fermentation tubes were used, containing sugar-free broth to which had been added 1 per cent. of the various sugars. A culture of Buxton's paratyphoid bacillus, and cultures of two paratyphoid bacilli recently studied in this laboratory by G. Bertnard Smith (16), were compared in parallel tests. The following table shows the percentages of gas formed from the various carbohydrates by these organisms:

	Dex-trose	Lac-tose	Sacch-arose	Mal-tose	Man-nite	Levu-lose	Dex-trin	Galac-tose
Bacillus from the present case.....	25	25	20	25	..	22
Buxton's paratyphoid bacillus	25	27	25	35	..	20
Smith's paratyphoid I	28
Smith's paratyphoid bacillus II.....	22	30	25	27	15	25

Neutral red agar.—After twenty-four hours the medium appeared yellow, except for a narrow band of red at the surface and at the bottom of the tube. After forty-eight hours the red band at the bottom of the tube had disappeared, but that at the surface still remained. After a lapse of ten days the tube was red, except for a slight yellow color at the bottom, the original color returning after fifteen days.

Serum reactions.—At autopsy, slides were made of the heart's blood, with a view to testing the action of the patient's serum on any organism that might be recovered. Owing to an accident, these dried-blood preparations were destroyed, and an important link in the chain of evidence concerning our paratyphoid bacillus is therefore lacking.

In making the agglutination tests there were used two cultures of *B. typhosus*, two of *B. coli*, and one culture each of *B. enteritidis*, *B. cholerae suis*, *B. paratyphosus* of Buxton, *B. icteroides* (Sanarelli), *B. dysenteriae*, and *B. fecalis alcaligenes*, together with the organism isolated from the present case. Sera from rabbits immunized against *B. coli*, *B. typhosus*, *B. dysenteriae*,

B. enteritidis, *B. paratyphosus* of Buxton, and the bacillus from this case, were tested with the various members of the colon, intermediate, and typhoid groups. In all agglutination tests an arbitrary time limit of two hours was set, in order that results obtained with the various organisms might be compared.

Serum from a rabbit immunized against *B. coli*, which agglutinated the homologous organism in dilutions of 1:400, gave no result when tested with either the organism from the present case, or with Buxton's *B. paratyphosus*. A typhoid serum of high agglutinative power, 1:12,000, gave a positive result with the paratyphoid bacillus from the case in dilutions of 1:25, but normal rabbit sera gave like results in dilutions of 1:10 and 1:15. Serum from a rabbit immune to *B. dysenteriae* agglutinated the homologous organism in dilutions of 1:5,000, but gave no result with the paratyphoid bacillus in dilutions above 1:10.

B. enteritidis serum, having an agglutinative strength of 1:7,000, gave negative results in all dilutions with both Buxton's paratyphoid bacillus and the organism from our own case.

Serum from rabbits immunized against Buxton's paratyphoid bacillus and against our own organism gave the following results: Buxton's paratyphoid serum of an agglutinative strength for its own organism of 1:40,000 gave a positive result with the paratyphoid bacillus from the case in dilutions up to 1:30,000. A dilution of 1:40,000 gave a negative result. Serum from this animal did not agglutinate the other members of the intermediate group that were tested, nor members of the colon and typhoid groups.

A serum, obtained by immunizing a rabbit against the organism from our case, agglutinated the homologous organism in dilutions up to 1:40,000, a dilution of 1:50,000 giving a negative result. Buxton's paratyphoid bacillus was agglutinated in dilutions up to 1:20,000; a dilution of 1:25,000 failed to agglutinate. *B. coli*, *B. enteritidis*, *B. cholerae suis*, *B. icteroides* (Sanarelli), *B. typhosus*, *B. dysenteriae*, and *B. fecalis* *alcaligenes* were not agglutinated by this serum in any dilutions. The following table shows the action of this serum upon four paratyphoid organisms.

The character of the organism isolated from the present case indicates that it is a paratyphoid bacillus belonging to group *a* of Buxton's classification.

	1:40	1:100	1:1,000	1:20,000	1:30,000	1:40,000	1:50,000
B. paratyphosus fr. the case	+	+	+	+	+	+	-
Buxton's B. para- typhosus.....	+	+	+	+	-	-	-
Smith's para ty- phoid I.....	+	+	-	-	-	-	-
Smith's para ty- phoid II.....	+	+	+	-	-	-	-

GENERAL SUMMARY.

Putting together these five cases, it is evident that paratyphoid infections are accompanied by changes quite different from those of typhoid. On the other hand, there is little characterizing this type of infection or differentiating it from other septicemias anatomically, however much it may differ clinically. The most constant change is the splenic enlargement, which was present in all five cases. In most respects this enlargement seems to be the same as that of typhoid or ordinary septicemia, and in our case the microscopic findings are also similar. The loading of the splenic endothelial cells with pigment and erythrocytes is evidently the result of the hemolysis of the disease. The intestinal lesions, however, are quite variable. Because of the occasional occurrence of intestinal hemorrhages, it had at first been thought that intestinal ulcers probably were present, although the first cases autopsied, those of Strong and Longcope, showed the intestines to be quite unaffected. In the last two cases, however, there have been numerous ulcers, although entirely different from those of typhoid. In our case, in which the hemorrhages were a prominent feature of the case, the largest amount of ulceration of any of the five was found. The reporters of the three cases in which ulcerations were described all agreed in likening the ulcers to those of dysentery rather than to those of typhoid. In all cases there was also a practical absence of any alterations of Peyer's patches or of the solitary follicles. Likewise the mesenteric glands are almost unaltered. Strong alone reports swelling of

the glands, which were not microscopically examined. Lucksch found one enlarged gland, with slight endothelial proliferation. In the other three there were no gross changes in them, and in none does there seem to have been any generalized glandular hyperplasia. In Longcope's case and in ours there were typical focal necroses in the liver, differing from those of typhoid in not containing endothelial cells. Beyond these changes there seem to be none of significance.

The anatomic changes, therefore, are simply those of a septicemia, with splenic swelling, and occasionally non-specific ulcerations in the intestine. This picture is, of course, altogether different from that of typhoid, excepting the cases of typhoid without intestinal lesions, and suggests that possibly some of the cases reported to be of this kind may have really been paratyphoid infections. The changes of proliferation and phagocytosis as described by Mallory (12) are almost entirely absent in the intestinal lesions when ulcers exist, and are very slight in the mesenteric glands, not being greater in our case than might be seen in any enteritis. The total escape of the Peyer's patches in all five cases suggests some essential, if obscure, biologic difference between the typhoid and paratyphoid organisms.

The slight alterations generally found in the intestines agrees with the clinical history in respect to intestinal symptoms, for Brion (2) found diarrhoea present in but 18 per cent. of the recorded cases. Hemorrhage was present in but 5 per cent. Hence it is quite probable that intestinal lesions may be even less frequent in the non-fatal cases than indicated in the five autopsies, since these last necessarily represent exceptionally severe types of the disease. That fatal paratyphoid cases are really rarities, rather than overlooked through imperfect bacteriologic study, is indicated by Lucksch's (11) experience, for his one paratyphoid case was the only one found among 102 autopsies of typhoid cases. Another interesting feature is the scattering of these five cases over the entire globe, occurring as they did in Santa Cruz, Bohemia, Roumania, Philadelphia, and Chicago, which indicates that the geographical distribution of the paratyphoid bacillus is as wide as that of the typhoid bacillus.

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EXPLANATION OF PLATE III.

FIG. 1.—Low-power drawing of the margin of one of the intestinal ulcers. The blue-staining area in the submucosa is the edge of a Peyer's patch, at the line of junction of the necrotic and sound tissue, showing the diffusion of the nuclear material as described in the text. With this exception, it will be noticed, there is a total absence of any line of demarkation, as well as of cellular reaction. The absence of proliferation is particularly striking if compared with Mallory's (12) plates.

FIG. 2.—High-power drawing of mesenteric lymph gland, showing one of the areas resembling focal necrosis. The pink-staining substance is fibrin. The absence of necrotic cells and proliferated endothelium is shown.

We are indebted to Miss E. P. Miller for the drawings.

PLATE III.

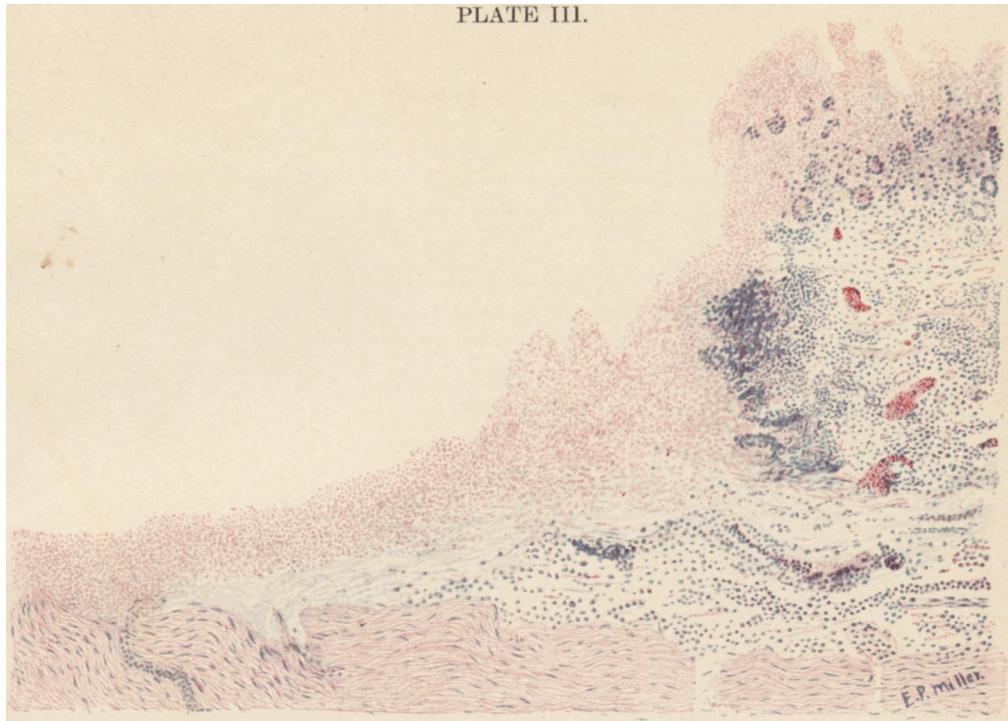


FIG. 1.

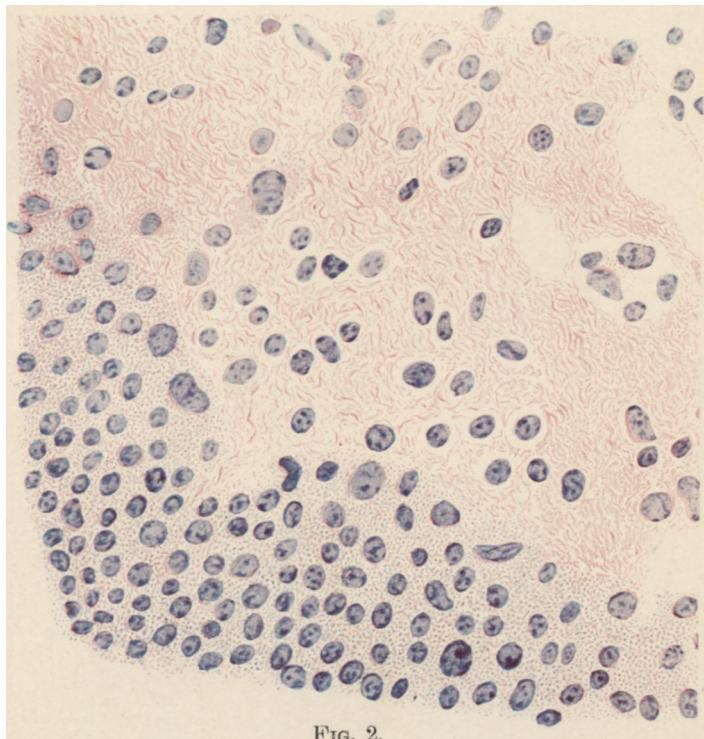


FIG. 2.